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(54) Title: CONTRAST AGENT ENHANCED MAGNETIC RESONANCE ANGIOGRAPHY WITH VESSEL SEGMENTATION		
<p>The diagram illustrates the acquisition of NMR images. A series of eight overlapping slices (301-308) are shown, representing a time-resolved phase of the examination. Below the slices is a horizontal timeline labeled 'ACQUIRED SEGMENT' with 14 segments: A1, B2, A3, C4, A5, B6, A7, C8, A9, D10, A11, E12, A13, F14. The timeline is divided into two phases: 'TIME RESOLVED PHASE' (covering segments A1 through C8) and 'STEADY STATE PHASE' (covering segments A9 through F14). Arrows indicate the correspondence between the slices and the segments on the timeline.</p>		
(57) Abstract <p>A magnetic resonance angiogram (RMA) is acquired using a contrast enhancement method in which a series of low resolution NMR images are rapidly acquired during a time resolved phase of the examination in which the contrast bolus makes a first pass through the arteries and veins. Additional, high resolution NMR image data is acquired in a subsequent steady-state phase of the examination from which a high resolution NMR image is reconstructed. Segmentation of arteries, veins and background in the high resolution image is performed using information in the low resolution NMR images.</p>		

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CONTRAST AGENT ENHANCED MAGNETIC RESONANCE ANGIOGRAPHY WITH VESSEL SEGMENTATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No.
5 60/115,259, filed January 8, 1999.

BACKGROUND OF THE INVENTION

The field of the invention is magnetic resonance angiography ("MRA"),
and particularly, studies of the human vasculature using contrast agents
10 which enhance the NMR signals.

Diagnostic studies of the human vasculature have many medical
applications. X-ray imaging methods such as digital subtraction angiography
("DSA") have found wide use in the visualization of the cardiovascular
system, including the heart and associated blood vessels. Images showing
15 the circulation of blood in the arteries and veins of the kidneys and the carotid
arteries and veins of the neck and head have immense diagnostic utility.
Unfortunately, however, these x-ray methods subject the patient to potentially
harmful ionizing radiation and often require the use of an invasive catheter to
inject a contrast agent into the vasculature to be imaged.

20 One of the advantages of these x-ray techniques is that image data
can be acquired at a high rate (i.e. high temporal resolution) so that a
sequence of images may be acquired during injection of the contrast agent.
Such "dynamic studies" enable one to select the image in which the bolus of
contrast agent is flowing through the vasculature of interest. Earlier images in
25 the sequence may not have sufficient contrast in the suspect vasculature, and
later images may become difficult to interpret as the contrast agent reaches
veins and diffuses into surrounding tissues. Subtractive methods such as that
disclosed in U.S. Patent No. 4,204,225 entitled "*Real-Time Digital X-ray
Subtraction Imaging*" may be used to significantly enhance the diagnostic
30 usefulness of such images.

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Magnetic resonance angiography (MRA) uses the nuclear magnetic resonance (NMR) phenomenon to produce images of the human vasculature. When a substance such as human tissue is subjected to a uniform magnetic field (polarizing field B_0), the individual magnetic moments of the spins in the tissue attempt to align with this polarizing field, but precess about it in random order at their characteristic Larmor frequency. If the substance, or tissue, is subjected to a magnetic field (excitation field B_1) which is in the x-y plane and which is near the Larmor frequency, the net aligned moment, M_z , may be rotated, or "tipped", into the x-y plane to produce a net transverse magnetic moment M_x . A signal is emitted by the excited spins, and after the excitation signal B_1 is terminated, this signal may be received and processed to form an image.

When utilizing these signals to produce images, magnetic field gradients (G_x , G_y and G_z) are employed. Typically, the region to be imaged is scanned by a sequence of measurement cycles in which these gradients vary according to the particular localization method being used. Each measurement is referred to in the art as a "view" and the number of views determines the resolution of the image. The resulting set of received NMR signals, or views, are digitized and processed to reconstruct the image using one of many well known reconstruction techniques. The total scan time is determined in part by the number of measurement cycles, or views, that are acquired for an image, and therefore, scan time can be reduced at the expense of image resolution by reducing the number of acquired views.

MR angiography (MRA) has been an active area of research. Two basic techniques have been proposed and evaluated. The first class, time-of-flight (TOF) techniques, consists of methods which use the motion of the blood relative to the surrounding tissue as a means for differentiating the NMR signal amplitude. The most common approach is to exploit the differences in signal saturation that exist between flowing blood and stationary tissue. Flowing blood, which is moving through the excited region, is continually refreshed by spins experiencing fewer RF excitation pulses and

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is, therefore, less saturated. The result is the desired image contrast between the high-signal blood and the low-signal stationary tissues.

MR methods have also been developed that encode motion into the phase of the acquired NMR signal as disclosed in U.S. Patent No. Re.

5 32,701. These form the second class of MRA techniques, which are known as phase contrast (PC) methods. Currently, most PC MRA techniques acquire two images, with each image having a different sensitivity to the same spin motion. Angiographic images are then obtained by forming either the phase difference or complex difference between the pair of velocity-encoded
10 images. Phase contrast MRA techniques have been extended so that they are sensitive to velocity components in all three orthogonal directions.

To enhance the diagnostic capability of MRA a contrast agent such as gadolinium can be injected into the patient prior to the MRA scan. As described in U.S. patent No. 5,417,213 the trick with this contrast enhanced
15 (CE) MRA method is to acquire the central k-space views at the moment the bolus of contrast agent is flowing through the vasculature of interest. Collection of the central lines of k-space during peak arterial enhancement is key to the success of a CE-MRA exam. If the central lines of k-space are acquired prior to the arrival of contrast, severe image artifacts can limit the
20 diagnostic information in the image. Alternatively, arterial images acquired after the passage of the peak arterial contrast are obscured by the enhancement of veins. In many anatomic regions, such as the carotid or renal arteries, the separation between arterial and venous enhancement can be as short as 6 seconds.

25 The short separation time between arterial and venous enhancement dictates the use of acquisition sequences of either low spatial resolution or very short repetition times (TR). Short TR acquisition sequences severely limit the signal-to-noise ratio (SNR) of the acquired images relative to those exams in which longer TRs are possible. The rapid acquisitions required by
30 first pass CE-MRA methods thus impose an upper limit on either spatial or temporal resolution. An additional detrimental effect of rapid imaging of the first pass of the bolus of contrast is the spurious modulation of k-space data

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resulting from the shape of the bolus of contrast. Current CE-MRA exams are of immense clinical utility, but due to the temporal-spatial limitations, they still fall short of x-ray DSA, the current "gold standard".

Ideally, angiograms should be acquired with techniques which allow longer scan times, after the first pass of the contrast bolus. For example, intravascular contrast agents can provide significant signal enhancement of the blood pool for over one hour. Images acquired after the first pass of the contrast agent in the so called "steady state" portion of the examination have the advantages of providing SNR and resolution increases limited only by patient motion. Even images acquired using currently available extravascular agents, which show only weak decay of plasma T1 shortening, may be improved by longer acquisitions acquired after the first pass of the bolus. Steady-state images permit excellent vessel delineation, although venous enhancement can severely limit arterial visualization reprojection images.

Clearly, an acquisition method which combines the excellent arterial-venous separation seen in first pass CE-MRA with the high resolution, high SNR images acquired in the steady-state is desirable. One approach is to acquire an angiogram without regard for the venous enhancement, and then remove the venous signal as a post-processing step. These venous removal techniques, which are referred to as vessel "segmentation", have been attempted by several researchers. Current methods of vessel segmentation, however, have proven to be of limited usefulness partially due to the difficulty in determining which voxels are artery and which are vein based solely on a spatial/geometric analysis of the vessels, or an analysis of their signal intensities.

SUMMARY OF THE INVENTION

The present invention is an improved CE-MRA method which employs the NMR data acquired during the first pass of a bolus of contrast agent through the region of interest ("ROI") to identify arteries, veins and unenhanced background tissue, and to use that time resolved information to segment NMR image data subsequently acquired during the steady state

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portion of the examination. The method uses a time resolved series of images acquired during the first pass of the contrast bolus to calculate arterial and venous contrast enhancement reference curves. These curves are used to determine which voxels in an image contain arteries and which contain
5 veins and those voxels which are unenhancing, background tissue or noise. The arterial/venous determination may then be used to suppress venous and background signal in a high resolution arterial image.

It has been discovered that the most powerful discriminator of arterial and venous signal is temporal in nature. For an intravenous injection, the
10 contrast agent will pass, as a bolus, through the imaged arterial vasculature prior to passage through the venous system. In addition, the shape of the contrast bolus is distorted as it passes from the arteries to the veins, the venous contrast enhancement curve being "flatter" than the arterial enhancement curve. Signal-verses-time contrast enhancement reference curves are
15 obtained from a region of interest (ROI) analysis of the time resolved images. The time course of these reference curves is compared to the time course of each voxel intensity in the same time resolved image series. The result of the comparison is to assign a value, or weight, to each voxel. The weights are proportional to how well the time course of the voxel intensities compares to
20 the time course of the arterial and venous reference curves. These weights can be used to segment images acquired during the steady-state phase of the scan.

An object of the invention is to provide a high resolution high SNR image of the human vasculature. NMR data may be acquired during the
25 steady-state phase of the scan from which high resolution and high SNR images may be reconstructed. Voxels in these images may be segmented, or weighted, such that background tissues are suppressed and either venous or arterial signals are suppressed to provide the desired clinical image.

Another object of the invention is to provide a high resolution time
30 course series of contrast enhanced vascular images. Peripheral k-space data acquired during the steady-state phase is segmented, and the segmented data is combined with the central k-space data acquired during the time

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resolved phase of the scan. A high resolution series of time resolved images are reconstructed from the combined k-space data. Since the central k-space data acquired during the first pass of the contrast bolus is employed, the series of images depict the inflow of contrast agent, while the depiction of vessel edges is provided by the segmented peripheral k-space data.

The foregoing and other objects and advantages of the invention will appear from the following description. In the description, reference is made to the accompanying drawings which form a part hereof, and in which there is shown by way of illustration a preferred embodiment of the invention. Such embodiment does not necessarily represent the full scope of the invention, however, and reference is made therefore to the claims herein for interpreting the scope of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a block diagram of an MRI system which employs the present invention;

Fig. 2 is a graphic representation of the pulse sequence employed in the preferred embodiment of the invention;

Fig. 3 is a graphic representation of k-space from which data is sampled when practicing the preferred embodiment of the invention;

Fig. 4 is a graphic representation of the order in which the k-space of Fig. 3 is sampled; and

Fig. 5 is a graphic representation of typical arterial and venous enhancement curves produced when practicing the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring first to Fig. 1, there is shown the major components of a preferred MRI system which incorporates the present invention. The operation of the system is controlled from an operator console 100 which includes a keyboard and control panel 102 and a display 104. The console 100 communicates through a link 116 with a separate computer system 107 that enables an operator to control the production and display of images on

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the screen 104. The computer system 107 includes a number of modules which communicate with each other through a backplane. These include an image processor module 106, a CPU module 108 and a memory module 113, known in the art as a frame buffer for storing image data arrays. The

- 5 computer system 107 is linked to a disk storage 111 and a tape drive 112 for storage of image data and programs, and it communicates with a separate system control 122 through a high speed serial link 115.

The system control 122 includes a set of modules connected together by a backplane. These include a CPU module 119 and a pulse generator

10 module 121 which connects to the operator console 100 through a serial link

125. It is through this link 125 that the system control 122 receives commands from the operator which indicate the scan sequence that is to be performed. The pulse generator module 121 operates the system components to carry out the desired scan sequence. It produces data which
- 15 indicates the timing, strength and shape of the RF pulses which are to be produced, and the timing of and length of the data acquisition window. The pulse generator module 121 connects to a set of gradient amplifiers 127, to indicate the timing and shape of the gradient pulses to be produced during the scan. The pulse generator module 121 also receives patient data from a
- 20 physiological acquisition controller 129 that receives signals from a number of different sensors connected to the patient, such as ECG signals from electrodes or respiratory signals from a bellows. And finally, the pulse generator module 121 connects to a scan room interface circuit 133 which receives signals from various sensors associated with the condition of the
- 25 patient and the magnet system. It is also through the scan room interface circuit 133 that a patient positioning system 134 receives commands to move the patient to the desired position for the scan.

The gradient waveforms produced by the pulse generator module 121 are applied to a gradient amplifier system 127 comprised of G_x , G_y and G_z

30 amplifiers. Each gradient amplifier excites a corresponding gradient coil in an assembly generally designated 139 to produce the magnetic field gradients used for position encoding acquired signals. The gradient coil assembly 139

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forms part of a magnet assembly 141 which includes a polarizing magnet 140 and a whole-body RF coil 152. A transceiver module 150 in the system control 122 produces pulses which are amplified by an RF amplifier 151 and coupled to the RF coil 152 by a transmit/receive switch 154. The resulting
5 signals radiated by the excited nuclei in the patient may be sensed by the same RF coil 152 and coupled through the transmit/receive switch 154 to a preamplifier 153. The amplified NMR signals are demodulated, filtered, and digitized in the receiver section of the transceiver 150. The transmit/receive switch 154 is controlled by a signal from the pulse generator module 121 to
10 electrically connect the RF amplifier 151 to the coil 152 during the transmit mode and to connect the preamplifier 153 during the receive mode. The transmit/receive switch 154 also enables a separate RF coil (for example, a head coil or surface coil) to be used in either the transmit or receive mode.

The NMR signals picked up by the RF coil 152 are digitized by the
15 transceiver module 150 and transferred to a memory module 160 in the system control 122. When the scan is completed and an entire array of data has been acquired in the memory module 160, an array processor 161 operates to Fourier transform the data into an array of image data. This image data is conveyed through the serial link 115 to the computer system
20 107 where it is stored in the disk memory 111. In response to commands received from the operator console 100, this image data may be archived on the tape drive 112, or it may be further processed by the image processor 106 and conveyed to the operator console 100 and presented on the display 104.

Although the present invention can be used with a number of different
25 pulse sequences, the preferred embodiment of the invention employs a 3D gradient recalled echo pulse sequence depicted in Fig. 2. The pulse sequence "3dfgre" available on the General Electric 1.5 Tesla MR scanner sold under the trademark "SIGNA" with revision level 5.5 system software was used. It was modified to collect data from multiple volumes so that the k-
30 space sampling patterns described below can be practiced.

Referring particularly to Fig. 2, an RF excitation pulse 220 having a flip angle of 60° is produced in the presence of a slab select gradient pulse 222

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to produce transverse magnetization in the 3D volume of interest as taught in U.S. patent No. 4,431,968. This is followed by a phase encoding gradient pulse 224 directed along the z axis and a phase encoding gradient pulse 226 directed along the y axis. A readout gradient pulse 228 directed along the x axis follows and a partial echo (60%) NMR signal 230 is acquired and digitized as described above. After the acquisition, rewinder gradient pulses 232 and 234 rephase the magnetization before the pulse sequence is repeated as taught in U.S. patent No. 4,665,365.

As is well known in the art, the pulse sequence is repeated and the phase encoding pulses 224 and 226 are stepped through a series of values to sample the 3D k-space depicted in Fig. 3. In the preferred embodiment, sixteen phase encodings are employed along the z axis and 128 phase encodings are employed along the y axis. For each particular y phase encoding, therefore, sixteen acquisitions with sixteen different z phase encodings are performed to sample completely along the k_z axis. This is repeated 128 times with 128 different y phase encodings to sample completely along the k_y axis. As will become apparent from the discussion below, the order in which this sampling is performed is important.

Sampling along the k_x axis is performed by sampling the NMR echo signal 230 in the presence of the readout gradient pulse 228 during each pulse sequence. It will be understood by those skilled in the art that only a partial sampling along the k_x axis is performed and the missing data is computed using a homodyne reconstruction or by zero filling. This enables the echo time (TE) of the pulse sequence to be shortened to less than 1.8 to 2.0 ms. and the pulse repetition rate (TR) to be shortened to less than 10.0 msec.

The implementation of the present invention can be broken down into three parts: image acquisition; voxel characterization; and image reconstruction. Each part will now be discussed.

Image Acquisition

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The image acquisition steps are a modification of the 3D MRA dynamic study disclosed in U.S. Pat. No. 5,713,358 issued February 3, 1998 and entitled *"Method for Producing A Time-Resolved Series of 3D Magnetic Resonance Angiograms During the First Passage of Contrast Agent"*. The
5 present method circumvents the usual spatial-temporal constraints by acquiring data at a high temporal resolution in one phase of the acquisition, the "time resolved phase", and acquiring data at a high spatial resolution in a separate, "steady-state phase" of the acquisition.

When a contrast agent is injected into the patient the bolus flows into
10 the ROI being imaged and sharply enhances the signal of arterial blood first as illustrated by curve 280 in Fig. 5. Shortly thereafter venous blood is enhanced as indicated by curve 282, and then the signal from both arterial and venous blood settles into a steady state of moderate enhancement for a relatively long period of time. The acquisition of NMR data according to the
15 present invention is divided into two phases, a "time resolved phase" in which low to moderate resolution images are acquired at a high image frame rate, and a "steady state phase" in which high resolution, low noise image data is acquired.

Referring particularly to Fig. 3, to accomplish this acquisition the k-
20 space to be sampled is divided into six segments, or regions, designated "A-F". The boundaries of these regions are concentric about the origin of k_z - k_y space and a central region "A" occupies the central k-space region. As is well known in the art, the "central" samples of k-space contain most of the information which determines overall image contrast, whereas the "peripheral"
25 k-space samples contribute detail to the reconstructed image, such as vessel edges.

The order in which k-space is sampled in the preferred embodiment of the invention is shown in Fig. 4. The first phase of the acquisition produces segments 1 through 8 which are reconstructed using an appropriate
30 interpolation scheme and fast Fourier transform to form image frames 301 through 308 in a time course series of images. The images 301-308 are of lower resolution than the final image, but their high temporal resolution allows

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for arterial and venous signal-versus-time contrast enhancement reference curves 280 and 282 to be produced as will be described below.

After the first pass of the contrast bolus, the peripheral k-space segments are acquired during a steady-state phase of the acquisition. Since
5 the contrast agent present in the blood is changing very slowly with time, it is possible to scan for a much longer time than that permitted by first pass bolus dynamics. Therefore, in the high resolution, steady-state phase of the acquisition, all the segments of k-space A-F are acquired multiple times. By averaging these multiply acquired regions, the SNR is increased at a rate of
10 \sqrt{N} , where N is the number of times a given segment is averaged. The steady-state acquisition need not be time-resolved, but instead has high resolution and much higher SNR at the cost of both arterial and venous opacification.

Many variations are possible from the preferred data acquisition
15 procedure described above. Other low resolution, high speed NMR pulse sequences can be used during the time resolved phase, and different NMR pulse sequences can be used during the steady-state phase. For example, spiral pulse sequences such as those described in U.S. Pat. No. 4,748,410, and projection acquisitions such as that described in co-pending U.S. Pat.
20 Appln. Serial No. _____, filed on _____ and entitled "*Phase Contrast Imaging Using Interleaved Projection Data*" may be used during the time resolved phase. The pulse sequence may be switched to another pulse sequence during the steady-state phase, or the same pulse sequence may be used in modified form. For example, the sampling of k-
25 space along the readout gradient axis may be limited to a central region of k-space during the time resolved phase to shorten the TR period and thereby further increase the time resolution. This same pulse sequence may be used during the steady-state phase with a much larger range of k-space sampling along the readout gradient axis to improve image resolution.

30 Variations are also possible in the segmentation of k-space and the order in which the segments are acquired. In one alternative embodiment, for example, the central segment A is set to a size such that only the A segment

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need be acquired during the time resolved phase. Such "key hole" acquired images must have a resolution sufficient to produce a contrast enhancement curve for each voxel therein with the required time and spatial resolution.

The present invention also enables the use of a broader range of
5 contrast agents. Intra-vascular contrast agents which provide prolonged signal enhancement following first pass through the arteries may be used.

Voxel Characterization

To use the high resolution data acquired during the steady-state phase of the acquisition, the voxels in the reconstructed image must be segmented
10 so that arteries and veins can be distinguished from each other and from the background tissues. This is done by comparing the signal at each voxel during the time resolved phase of the acquisition with arterial and venous contrast enhancement reference curves. The contrast enhancement reference curves are produced using selected voxels from the time resolved
15 images 301-308. This is accomplished by manually selecting voxels in the respective images which lie within arteries and selecting voxels which lie within veins. The contrast enhancement reference curves 280 and 282 are produced by averaging the brightness values of the selected arterial and venous voxels in the successive time course images 301-308. These
20 contrast enhancement reference curves 280 and 282 will depend on injection rate, dose volume, anatomic region and the patients health, and therefore must be determined for each exam. The preferred implementation relies on a region-of-interest (ROI) analysis of the time series to provide two signal-versus-time contrast enhancement reference curves, one arterial and one
25 venous.

The signal changes at each voxel in the time resolved images 301-308 is compared with the contrast enhancement reference curves 380 and 382 to determine if it depicts arterial, venous or background tissue. Those voxel signals which closely follow the arterial reference curve 280 are designated
30 "arterial" and those voxel signals which correlate well with the venous reference signal 282 are designated "venous".

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The method of comparison is the Sum of Squared Deviations method (SSD). SSD sums the squared difference between the reference curve and the voxel brightness value, over all the time frames 301-308 acquired during the time-resolved phase of the examination. For a given voxel,

$$5 \quad SSD(voxel) = \sum_{frames} (REF(frame) - Voxel(frame))^2, \quad (1)$$

where REF(frame) is the value of the reference curve for a given image frame, and Voxel(frame) is the signal intensity of the voxel for the same image frame. The size of the SSD value reflects how well the voxels match up with the reference curves. Voxels which match closely to the reference
10 curves will have very small SSD values. Larger SSD values correspond to voxels whose time course brightness does not match the curves. Such voxels form part of the background tissues.

A problem with using a single measurement of the SSD value is that some venous voxels will have values which look more like arterial voxels than
15 true arterial voxels and vice versa. This problem is addressed by comparing each image voxel to both the arterial and the venous contrast enhancement reference curves 280 and 282 to obtain two SSD values (SSD_A and SSD_V) for each image voxel. The shape of the voxel signal curve is also sensitive to the absolute signal level measured at any voxel. The absolute signal is affected
20 by, among other things, coil sensitivity and vessel size. To account for these differences a scaled version of the voxel signal verses time curve is used. The scaling of the voxel values minimizes the SSD and thus provides an optimal SSD value.

The nature of each voxel in the acquired images can be characterized
25 using the calculated SSD_A and SSD_V values. Those image voxels with SSD_A values lower than a preset amount and lower than their SSD_V value may be characterized as arterial. Similarly, voxels with SSD_V values below a preset amount and lower than their SSD_A value may be characterized as venous. All other voxels may be characterized as background tissues.

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Rather than simply removing background from an arterial and/or venous MRA image, which gives the image an artificial look, the signal value of the unwanted background voxels may be suppressed by a weighting factor which ranges from 0 to 1. This gives the image a much more aesthetic look.

- 5 The SSD_A and SSD_V values are used to calculate these weights. The preferred embodiment determines a weight factor based upon the voxel's "distance" in a 2D (SSD_A , SSD_V) plane, from minimum calculated SSD_A and SSD_V values for the exam:

$$D(pixel) = \sqrt{(SSD_A(pixel) - SSD_A(MIN))^2 + (SSD_V(pixel) - SSD_V(MIN))^2} \quad (2)$$

- 10 where: SSD_A (voxel) = SSD_A for the subject voxel;
 SSD_V (voxel) = SSD_V for the subject voxel;
 SSD_A (MIN) = lowest SSD_A of any voxel in the images 301-308;
 SSD_V (MIN) = lowest SSD_V of any voxel in the images 301- 308.

- The distance (D) then is used to define a weight for each image voxel which
 15 is calculated analytically for each exam or which is rapidly determined by using a lookup table of previously calculated values.

- The time resolved segmentation method of the present invention can be used in combination with other segmentation methods to further characterize ambiguous image voxels. In the preferred embodiment this
 20 includes a spatial/geometric segmentation method as well as a signal analysis method. The spatial/geometric segmentation method employs an image in which the vascular voxels have been identified using the time resolved segmentation method described above. The location of ambiguous voxels is used to determine if they are part of a vessel. If the location of the
 25 ambiguous voxel is adjacent an identified vessel, it is characterized as part of the vessel if its signal level exceeds a threshold level. If it is located remotely from any vessel it is characterized as noise or background tissue. This method resolves the ambiguity with respect to voxels that connect with identified vessels.

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For ambiguous voxels which cannot be characterized by the connectivity method, a signal analysis method may be employed to further refine the segmentation. A region of voxels (e.g. 10 by 10 voxels) surrounding the ambiguous voxel is selected and a histogram of the signal levels in the time-resolved image having peak arterial contrast enhancement is produced. As illustrated in Fig. 6, the histogram indicates the number of voxels at each possible signal level, and a peak will occur when many voxels of substantially the same signal level are present in the region. A voxel number threshold is set at 20% of the peak number of voxels as indicated by dashed line 286. If the signal amplitude of the ambiguous voxel lies within the greater than 20% range of this peak as indicated at 288, it is characterized as a vessel.

Image Reconstruction

A number of different images may be constructed from the acquired NMR data and the voxel characterization information. Two preferred image reconstructions will now be described, but others are also possible. The first preferred embodiment is a method for reconstructing a single, high resolution and low noise image of the chosen vasculature (i.e. arteries, veins, or both arteries and veins). The second preferred embodiment is a method for reconstructing an enhanced set of time course image frames which depict the arrival of the contrast bolus in the subject vasculature.

Single Image

The objective of this method is to produce a single high quality image by combining all of the NMR data acquired during the two phases of the scan. Referring particularly to Fig. 7, the first step is to combine all the acquired k-space data segments into a single 3D k-space data set as indicated at process block 316. This combination can be as simple as the average value of each k-space sample in corresponding segments A-F. The greater the number of k-space samples in this average, the higher the SNR of the reconstructed image.

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The k-space samples from each acquired segment can also be combined in a weighted average. During data acquisition the various k-space segments are weighted by the contrast present at the time of their acquisition. For example, suppose A, B and C are three acquired k-space segments. For purposes of illustration we assume that a total of i A segments, j B segments and k C segments are acquired, the simplest composite image would be formed by averaging the various A, B and C segments separately prior to reconstruction. A better method is to form a matched filter in which each segment is weighted in proportion to the detected signal. Each detected A segment is related to the actual k-space segment A by the relationship $A_i = c_i A'$ where the subscripts refer to the time ordering of the various acquired A segments. The matched filter would further weight each A segment by c_i . The sum of weighted A segments would be normalized by dividing by the sum of the weighting coefficients used. The overall matched filter sum would be given by

$$\frac{\sum_i c_i(t) A_i(t)}{\sum_i c_i(t)} + \frac{\sum_j c_j(t) B_j(t)}{\sum_j c_j(t)} + \frac{\sum_k c_k(t) C_k(t)}{\sum_k c_k(t)} = \frac{\sum_i c_i^2(t) A'}{\sum_i c_i(t)} + \frac{\sum_j c_j^2(t) B'}{\sum_j c_j(t)} + \frac{\sum_k c_k^2(t) C'}{\sum_k c_k(t)}$$

It is also possible to generate a reweighted image in which the k-space filter caused by the contrast curve is removed in an attempt to increase spatial resolution at the possible expense of boosting high spatial frequency noise. This reweighted image is formed by multiplying the matched filter sums for each k space segment by an appropriate factor. It can be seen from the equation above that, for example, the A' portion of k-space in the matched filter sum is weighted by

$$\frac{\sum_i c_i^2(t)}{\sum_i c_i(t)}$$

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Therefore, each matched filter segment sums must be divided by this factor to completely remove contrast weighting. This results in a final matched filtered, re-weighted image given by

$$I_{RW} = \frac{\sum_i c_i(t) A_i(t)}{\sum_i c_i^2(t)} + \frac{\sum_j c_j(t) B_j(t)}{\sum_j c_j^2(t)} + \frac{\sum_k c_k(t) C_k(t)}{\sum_k c_k^2(t)}$$

- 5 This formula can be generalized to include a number of k-space segments. In addition, the weighted average for each segment A-F can be reweighted as described in U.S. Pat. No. 5,881,728, issued march 16, 1999 to account for changes in contrast enhancement during the scan.

As indicated at process block 318, the next step is to reconstruct an
 10 image from the combined k-space data set. This is a three-dimensional Fourier transformation followed by the calculation of the magnitude of each voxel in the image from its complex I and Q components. The operator then selects the object to be displayed in this image, the arteries, the veins, or both as indicated at process block 320.

- 15 As indicated at process block 322, the next step is to segment the 3D image. This is accomplished using the voxel characterization information described above and it can be done in two ways. First, the undesired structures can be totally eliminated from the image by forming a binary mask having bits corresponding to the image voxels. The voxel characterization
 20 information is used to set the mask bits to either "1" or "0" depending on whether the corresponding voxel is characterized as artery, vein or background. For example, if arteries are to be displayed, the mask bits characterized as artery are set to "1" and the remaining bits are set to "0". The voxel values in the combined 3D image are multiplied by their
 25 corresponding mask bits to produce the desired segmented 3D image.

Instead of totally masking out background voxels, it is also possible to segment the image by applying the weighting factors (D) calculated above to corresponding voxels in the combined 3D image. Rather than multiplying

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each background voxel by "0" and rendering it black, therefore, each background voxel is reduced in brightness by an amount determined by its weighting factor (D).

For assessing overall blood vessel structure and health it is usually
5 more useful to project the 3D array of image data into a single 2D projection image as indicated at process block 324. The most commonly used technique for doing this is to project a ray from each voxel in the projection image through the 3D array of image data points and select the data point which has the maximum value. The value selected for each ray is used to
10 control the brightness of its corresponding voxel in the 2D projection image. This method, referred to as the "maximum voxel technique," is very easy to implement and it gives aesthetically pleasing images.

Another technique which is used to form a 2D projection image and which retains more of the available information is what is referred to as the
15 "integration method". This projection method is described in U.S. patent No. 5,204,627 entitled "Adaptive NMR Angiographic Projection Method" and is incorporated herein by reference. With this method the brightness of each projection image voxel is determined by the sum of all the data points along the projection ray.

20 Time Course Image Frames

The NMR data acquired during the steady-state phase of the scan can also be used to improve the quality of the image frames 301-308 acquired during the time-resolved phase. These enhanced time course images can be viewed in sequence to observe the arrival of the contrast bolus in the
25 vasculature.

Referring to Fig. 8, the first step is to produce a segmented image using only k-space data segments acquired during the steady-state phase of the scan as indicated at process block 330. This segmented image is produced in the same manner described above for the single image
30 reconstruction, but no time-resolved data segments are used. This segmented image is Fourier transformed back to k-space as indicated at

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process block 332 and the peripheral k-space segments from the resulting k-space data set are selected out and combined with the central k-space segments acquired during the time resolved phase as indicated at process block 334. That is, the segmented k-space data for peripheral segments D, E
5 and F are combined with the time course k-space data segments A, B and C. The enhanced time course images are reconstructed from this combined k-space data by performing a 3D Fourier transformation as indicated at process block 336.

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Claims

1. A method for producing a magnetic resonance angiogram of a patient using an MRI system, the steps comprising:
 - a) injecting the patient with a contrast agent which flows into a region of interest in the patient;
 - 5 b) acquiring NMR image data for a series of NMR time course images during a time resolved phase of an examination, during which the contrast agent makes a first passage through the patient's arteries in the region of interest;
 - c) acquiring NMR image data during a steady state phase of the examination which follows the time resolved phase;
 - 10 d) reconstructing an image from NMR data acquired during the examination;
 - e) producing the magnetic resonance angiogram by segmenting the image reconstructed in step d) using information contained in the series of
 - 15 NMR time course images.
2. The method as recited in claim 1 in which the segmentation includes reducing the brightness of voxels in the image which do not depict arteries.
3. The method as recited in claim 1 which includes producing from the NMR time course images an arterial enhancement reference curve that indicates the signal level enhancement of image voxels depicting arteries during the time resolved phase of the examination, and the segmenting in
- 5 step e) employs the arterial enhancement reference curve.

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4. The method as recited in claim 3 which includes producing from the NMR time course images a venous enhancement reference curve that indicates the signal enhancement of image voxels depicting veins during the time resolved phase of the examination, and the segmenting in step e)
- 5 employs the venous enhancement reference curve.

5. The method as recited in claim 3 in which the segmenting in step e) includes comparing the brightness levels of each image voxel during the time resolved phase of the examination with corresponding points in the arterial enhancement reference curve and modifying the brightness of the
- 5 voxel in the magnetic resonance angiogram as a function of this comparison.

6. The method as recited in claim 1 in which the segmenting in step e) includes:
- i) producing from the NMR time course images an arterial enhancement reference curve that indicates the signal level enhancement of
 - 5 image voxels depicting arteries during the time resolved phase of the examination;
 - ii) comparing each voxel signal level enhancement in the NMR time course images with the arterial enhancement reference curve and producing a correlation value SSD_A for each such voxel;
 - 10 iii) producing from the NMR time course images a venous enhancement reference curve that indicates the signal level enhancement of image voxels depicting veins during the time resolved phase of the examination;
 - iv) comparing each voxel signal level enhancement in the NMR
 - 15 time course images with the venous enhancement reference curve and producing a correlation value SSD_V for each such voxel; and
 - v) each corresponding voxel in the reconstructed image is characterized by evaluating the correlation values SSD_A and SSD_V .

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7. The method as recited in claim 3 in which the signal levels of voxels in the series of NMR time course images are compared with the arterial enhancement reference curve to characterize image voxels depicting arteries as arterial voxels, and the segmenting of the image reconstructed in
5 step d) includes selecting for inclusion in the magnetic resonance angiograms image voxels therein which correspond to arterial voxels.

8. The method as recited in claim 7 in which the segmenting of the image reconstructed in step d) includes suppressing the signal level (D) of voxels therein which are not characterized as arterial voxels.

9. The method as recited in claim 1 in which the image reconstructed in step d) is formed using NMR image data acquired during the time resolved phase and during the steady-state phase of the examination.

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10. A method for producing a magnetic resonance angiogram of a patient using an MRI system, the steps comprising:
- a) injecting the patient with a contrast agent which flows into a region of interest in the patient;
 - 5 b) acquiring NMR central k-space data for a series of NMR time course images during a time resolved phase of an examination, during which the contrast agent makes a first passage through the patient's arteries in the region of interest;
 - c) acquiring NMR k-space data during a steady state phase of the examination which follows the time resolved phase;
 - 10 d) characterizing voxels in the NMR time course images that depict arteries by analyzing the signal level enhancement of each voxel caused by the contrast agent;
 - e) reconstructing an image using NMR k-space data acquired
 - 15 during the steady-state phase of the examination; and
 - f) segmenting the reconstructed image by suppressing signals from voxels that have not been characterized as arterial.
11. The method as recited in claim 10 in which NMR k-space data is repeatedly acquired during the steady-state phase of the examination to produce multiple k-space samples and the multiple k-space samples are combined to form average k-space samples.
12. The method as recited in claim 11 in which the multiple k-space samples are combined to form weighted average k-space samples.

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13. The method as recited in claim 10 in which step b) is performed by:

repeatedly performing a first NMR pulse sequence which acquires NMR central k-space data at a high temporal rate;

5 and step c) is performed by:

repeatedly performing a second NMR pulse sequence which acquires NMR k-space data from which a high resolution image may be reconstructed.

14. The method as recited in claim 10 which includes:

g) combining data from the segmented reconstructed image with each of a plurality of the NMR time course images to produce enhanced NMR time course images.

15. The method as recited in claim 14 in which step g) includes:

i) Fourier transforming the segmented reconstructed image to produce a segmented k-space data set;

5 ii) combining peripheral k-space data from the segmented k-space data set with the NMR central k-space data acquired in step b); and

iii) reconstructed the plurality of NMR time course images from the k-space data combined in step ii).

16. The method as recited in claim 13 in which the first NMR pulse sequence includes sampling k-space in a spiral trajectory.

17. The method as recited in claim 13 in which the first NMR pulse sequence includes sampling k-space from a projection angle and the projection angle is changed for each repetition of the first NMR pulse sequence.

18. The method as recited in claim 13 in which the first NMR pulse sequence includes applying phase encoding gradients which sample k-space in a centric order as the first NMR pulse sequence is repeated.

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19. The method as recited in claim 10 in which the contrast agent is an intra-vascular material which enhances the NMR signals in the patient's vasculature for a substantial period of time.

20. The method as recited in claim 19 in which the contrast agent is an intra-vascular contrast agent.

21. The method as recited in claim 10 which includes:

h) characterizing voxels in the NMR time course images that depict veins by analyzing the signal level enhancement of each voxel caused by the contrast agent.

22. The method as recited in claim 21 in which the analyzing in step d) includes:

- i) producing from the NMR time course images an arterial enhancement reference curve that indicates the signal level enhancement of image voxels depicting arteries during the time resolved phase of the examination;
- ii) comparing each voxel signal level enhancement with the arterial enhancement reference curve and producing a correlation value SSD_A for each voxel; the analyzing in step g) includes:
- iii) producing from the NMR time course images a venous enhancement reference curve that indicates the signal level enhancement of image voxels depicting veins during the time resolved phase of the examination;
- iv) comparing each voxel signal level enhancement with the venous enhancement reference curve and producing a correlation value SSD_V for each voxel; and
- v) each voxel is characterized by evaluating the correlation values SSD_A and SSD_V .

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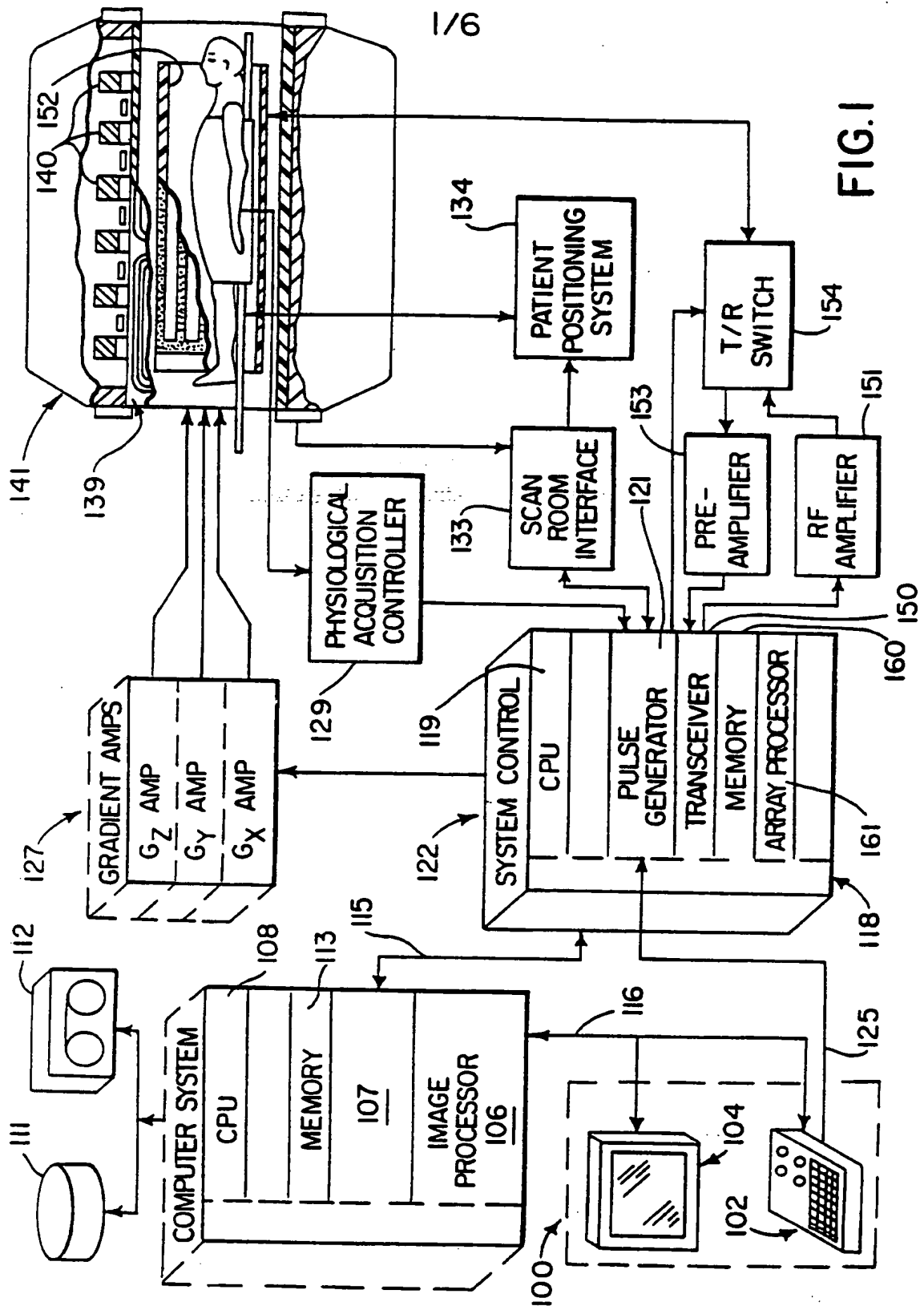
23. The method as recited in claim 22 in which step v) includes: evaluating the spatial location of the voxel relative to other voxels characterized as arterial.

24. The method as recited in claim 22 in which step v) includes: evaluating the level of the voxel signal relative to the signal level of surrounding voxels.

25. The method as recited in claim 10 in which step f) includes:
i) producing a binary mask which indicates the voxels characterized as depicting arteries; and
ii) combining the binary mask with the reconstructed image to
5 suppress the signals from non-arterial voxels.

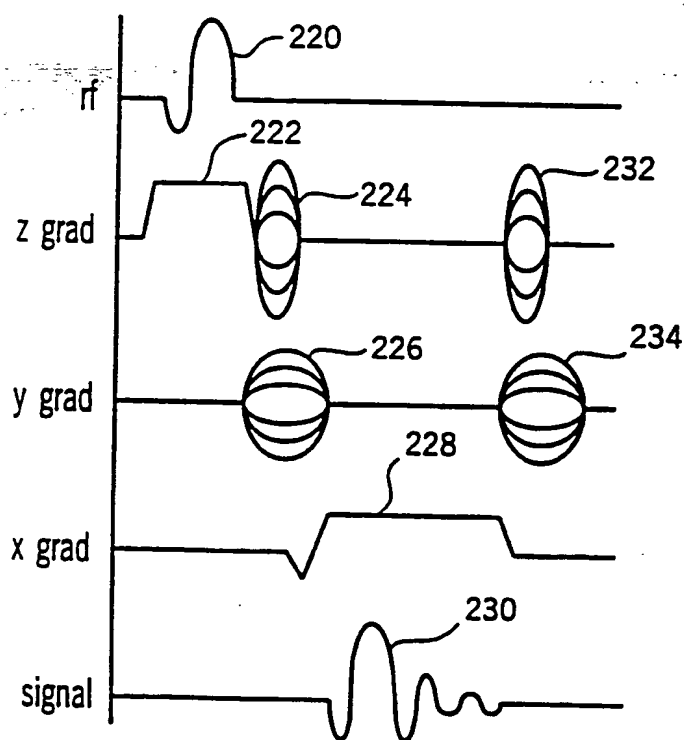
26. The method as recited in claim 25 in which the non-arterial voxel signals are set to zero.

27. The method as recited in claim 10 in which step d) includes calculating a weighting factor D for each voxel in the NMR time course images; and step f) includes multiplying each voxel by its corresponding weighting factor D.



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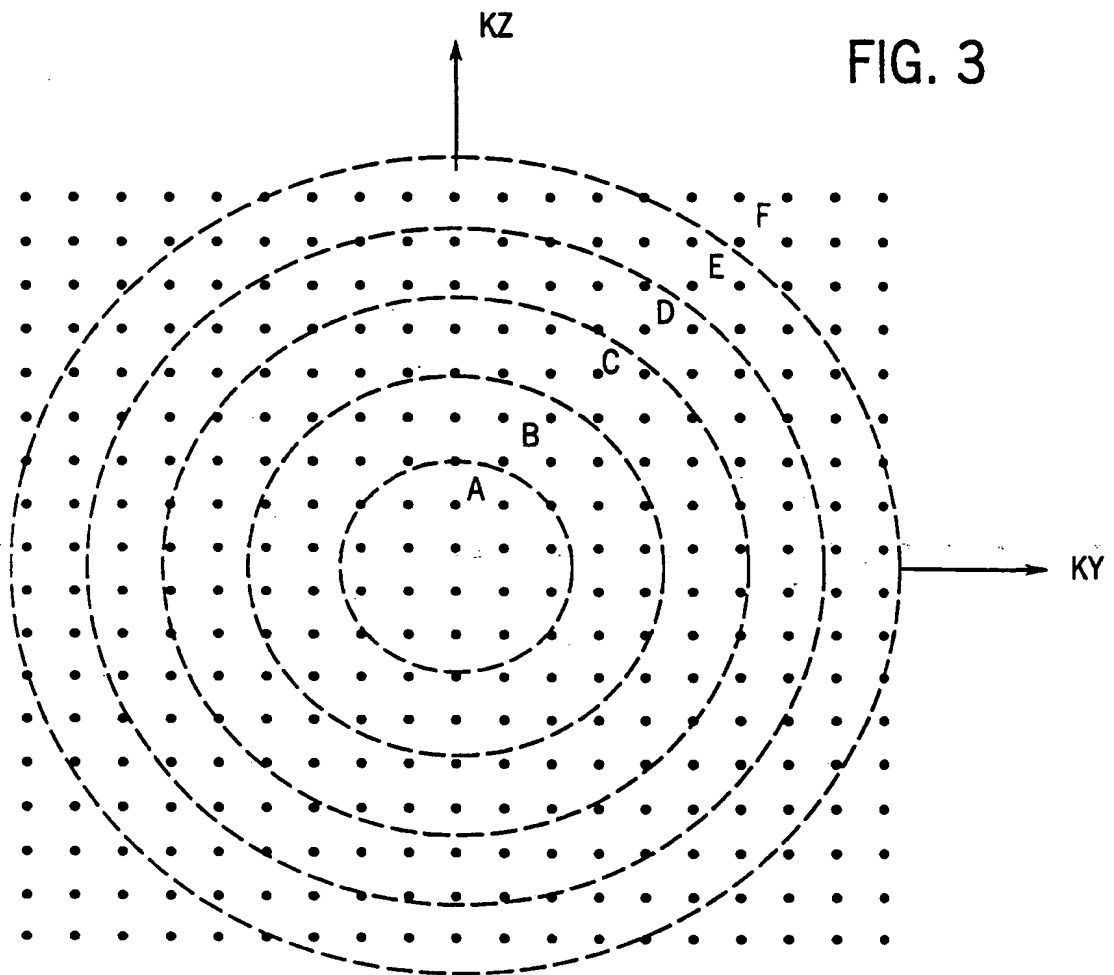
FIG. 2



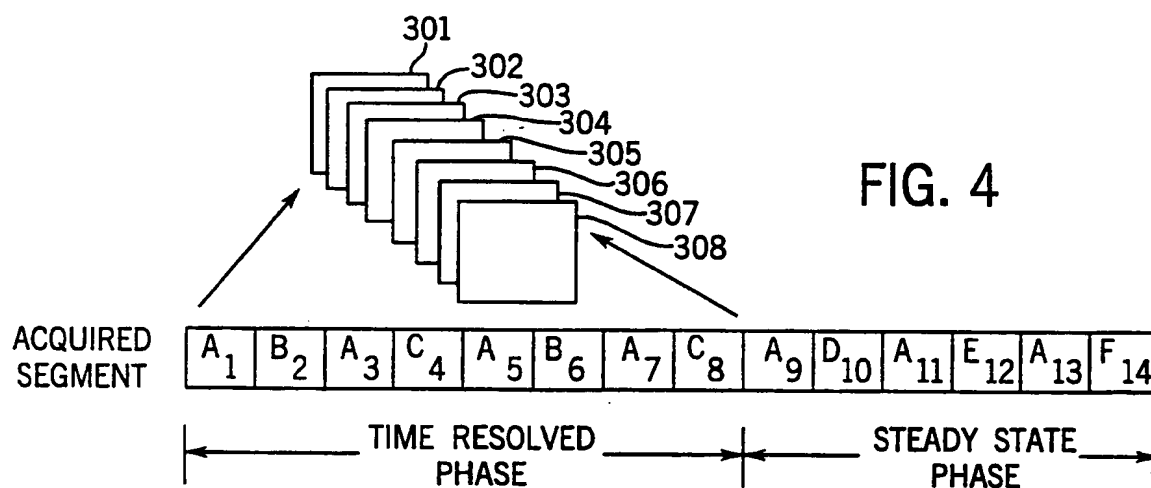
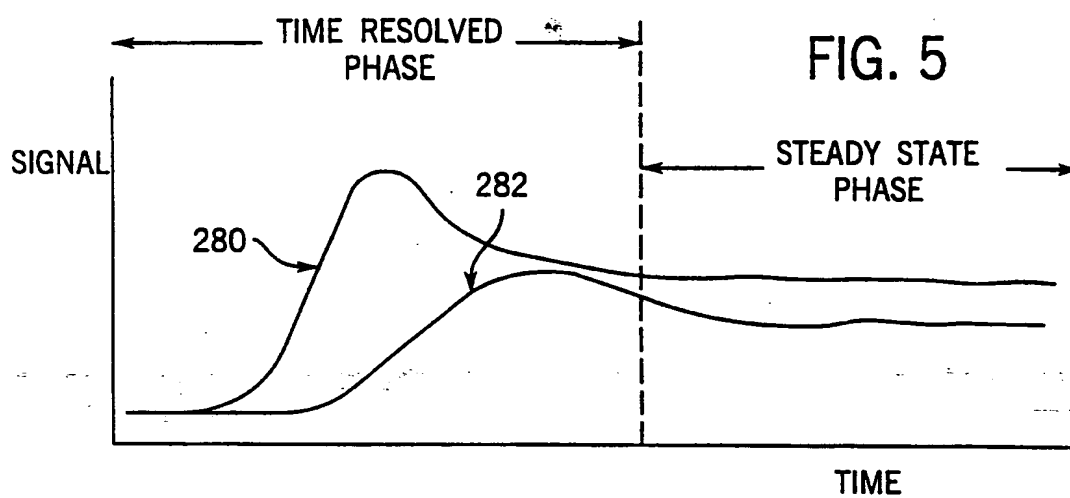
3/6

KZ

FIG. 3

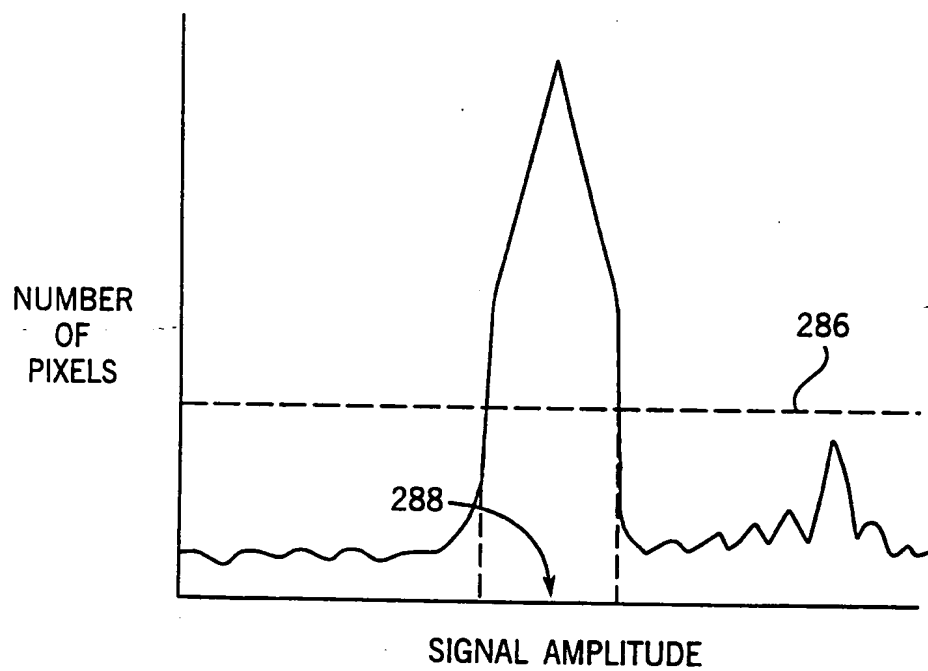


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FIG. 6



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FIG. 7

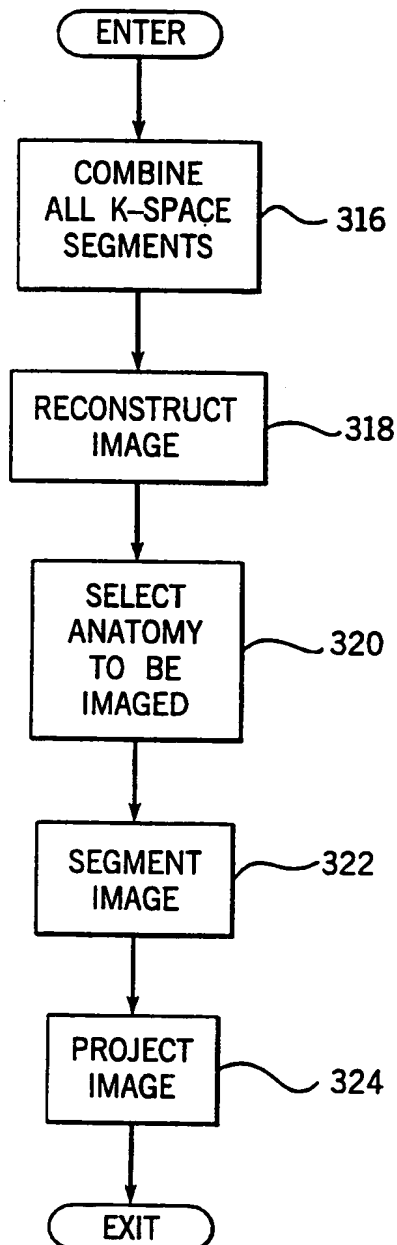
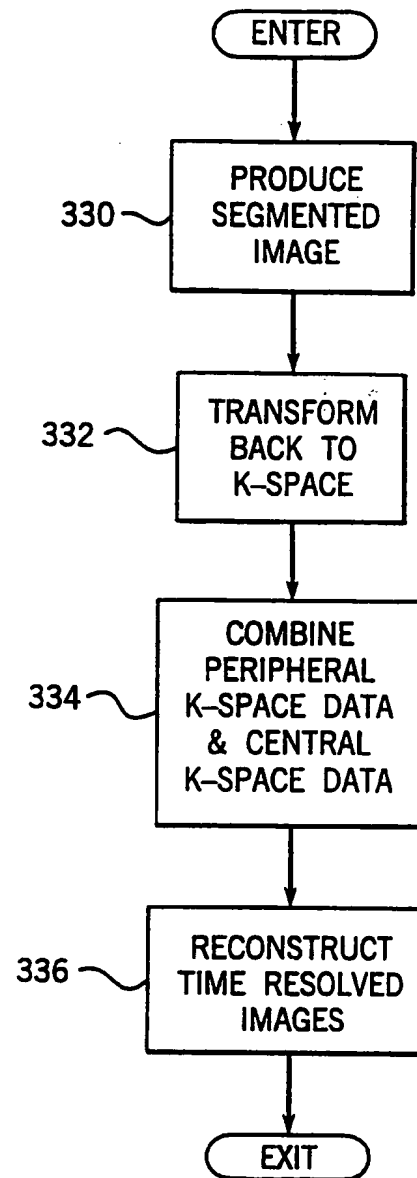


FIG. 8



INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/00137

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01R33/563

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01R

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	O.SIMONETTI ET AL.: "A Method of Distinguishing Arteries and Veins in Intra-Vascular Contrast Agent Enhanced MR Angiography" PROCEEDINGS OF THE INTERNATIONAL SOCIETY FOR MAGNETIC RESONANCE IN MEDICINE, SIXTH SCIENTIFIC MEETING AND EXHIBITION, SYDNEY, AUSTRALIA, APRIL 18-24, 1998, vol. 2, page 777.XP002136099 see the whole abstract --- -/--	1-27

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

20 April 2000

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

i. national Application No
PCT/US 00/00137

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	D.W.KAANDORP ET AL.: "Improving the performance of 3D dynamic Gd-enhanced carotid artery imaging using the Eigenimage filter" PROCEEDINGS OF THE INTERNATIONAL SOCIETY FOR MAGNETIC RESONANCE IN MEDICINE, SIXTH SCIENTIFIC MEETING AND EXHIBITION, SYDNEY, AUSTRALIA, APRIL 18-24, 1998, vol. 1, page 566 XP002136100 see the whole abstract ---	1-27
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INTERNATIONAL SEARCH REPORT

Information on patent family members

In. tional Application No

PCT/US 00/00137

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